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10/049,704	05/16/2002	Camilo Anthony Leo Selwyn Colaco	8830-21	7595

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	PAPER NUMBER
1645	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/049,704	COLACO, CAMILO ANTHONY LEO SELWYN	
	Examiner	Art Unit	
	GINNY PORTNER	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 17* is/are pending in the application.

4a) Of the above claim(s) *1-9 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-14, 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-9 and 15 stand withdrawn from consideration.
Amended claims 10-14 and 17 are currently under examination.

Rejections Withdrawn

1. Claim 10 under 35 U.S.C. 102(b) as being anticipated by Rambukkana et al (Nov. 1992) is herein withdrawn in light of the amendment of the claim and Applicant's traversal.

Response to Arguments for Rejections Maintained

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

1. ***(Rejection Maintained) Claim Rejections - 35 USC § 102***: The rejection of claims 10-14, and claim 17 under 35 U.S.C. 102(e) as being anticipated by Srivastava (US 5,961,979) is traversed on the grounds that: Srivastava teaches "the use of mammalian HSP-complexes from infected cells as vaccines against intracellular pathogens" and the instant invention is directed to complexes in which "Both the heat shock protein and the antigenic peptide fragment are derived from the same cell, a pathogenic bacterium."

2. It is the position of the examiner that Srivastava disclose compositions that comprise Bacterial/E.coli heat shock protein-peptide complexes from bacteria through disruption of the bacterial pathogen and then naturally purified and include peptides that "originate from the pathogen itself" (see col. 6, lines 12-13; col. 6, lines 65-68 and col. 7, line 7). Srivastava's heat shock proteins are not limited to mammalian heat shock proteins. Srivastava discloses DnaK and Hsp70 from E.coli (see col. 5, line 57), and heat shock proteins (see Table 1, col. 16, Hsp60, Hsp70 and Hsp90 from E.coli) from other pathogens as well. The heat shock proteins of Srivastava are defined as "a protein whose intracellular concentration increases when a cell is exposed to a stressful stimuli, it is capable of binding other proteins or peptides and it is capable of releasing the bound proteins or peptides in the presence of adenosine triphosphate (ATP) or low pH." (see col. 11, lines 4-10). The examiner agrees that the antigenic peptide fragment in the complexes of Srivastava are those claimed by Applicant (see Srivastava col. 6, lines 41-45; col. 5, lines 20-22; col. 7, lines 3-5; col. 6, line 67) and would originate from the same bacterium (see col. 6, lines 12-13).

Srivastava discloses the claimed compositions produced by a stress process and isolated

form natural sources, produced in situ. The bacterial heat shock protein (see Table 1 and definitions) is complexed together with an antigenic peptide fragment from a bacteria (see col. 7, line 7 "Chlamydia"), fungus, or protozoa, wherein the heat shock protein complex is isolated from natural sources (see col. 21, line 28).

1. The instantly claimed compositions are defined by the recited product by process limitations, but may be produced by a different process that produces the same or equivalent product and are not limited to the compositions produced in Examples 3 and 4. *See In re Mills*, 470 F.2d 649, 651, 176 (USPQ 198 (CCPA 1972).

2. Traversal directed to mammalian heat shock protein-peptide complexes are not convincing in light of the fact that Srivastava discloses compositions of heat shock proteins complexed with a peptide that originates from the bacterium in situ. Srivastava still anticipates the instantly claimed invention as now claimed, in light of the fact that the instant claims are not limited to complexes from extra cellular bacteria and the heat shock protein/peptide complexes are disclosed in Srivastava to be obtainable from natural sources through disruption of the bacterial cells.

Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594 No side by side comparisons have been submitted to show the novel or unobvious difference between the claimed compositions and the product of the prior art.

3. The rejection of claims 10-14 and 17 rejected under 35 U.S.C. 102(b) as being anticipated by Phipps et al (1991) is traversed on the grounds that the Phipps et al complex is "almost completely uncharacterized" other than the fact that the complex results following heat shock.

4. It is the position of the examiner that Applicant's heat shock complex results from the same process as that of Phipps et al, namely heat shock. No specific proteins of any specific relative molecular weight or structure are required by the instant claims, therefore the disclosure of Phipps et al meets the requirements of the claims directed to compositions that comprise a heat shock protein/peptide complex produced by heat shock and is accomplished in an ATP-dependent reaction (see title "ATPase complex") because the E. coli and Pyrodictium ATPase complexes produced multiple bands (see Fig. 9), to include two immunoreactive protein bands upon gel electrophoresis (see Figure 10).

5. Figures 9 and 10 show proteins present in the heat shock complexes from bacteria, to include E.coli (see Fig. 10, lane h). Each of the ATPase complexes when solubilized, run on a gel, and visualized with antibodies directed against purified ATPase complex; each complex visualized comprising/showing at least two protein bands. On page 1718, col. 2, paragraph 1, E.coli GroEL is characterized to be an abundant heat shock protein which possess ATPase activity and evidenced a band on the gel shown in figure 10 of a relative molecular weight of about 57kDa; the gel also shows an additional E.coli band that is present in the complex of 62 kDa. Additionally, Phipps et al teach that the ATPase protein complex exists "in the cell as two polypeptides of similar mol. Wt, i.e., this is not the result of proteolysis during purification", and

therefore discloses a heat shock protein complex that comprises two proteins/peptides (see page 171, col. 2, paragraph 2, whole paragraph).

6. The heat shock protein complexes were produced in response to heat shock (see Figure 10, page 171) and shown to be cross reactive with antibodies raised to GroEL (page 1718, col. 2, middle of paragraph) and immunoreactive with antibodies against purified ATPase complex (see Figure 10, page 171) Therefore Phipps et al still disclose the instantly claimed invention directed to:

Instant claim 10, 17: a complex of a heat shock protein that requires ATP for the formation of the complex that comprises a heat shock protein together with a peptide (see page 1711, title "Novel ATPase complex selectively accumulated upon heat shock"; E.coli: page 171, col. 2, "membrane free French press lysates" including E.coli. The Ecoli complex possessed ATPase activity (see page 1718, col. 1, paragraph 1, was immunocross reactive , Table 1, and Figure 10, lane h E.coli), and the "level of the complex in the cell is elevated following heat shock (see page 1711, col. 2, paragraph 1; see page 1713, col. 1, paragraph 2 "several different particles"; see page 1717, col. 1, paragraph 1 "73% of the total soluble protein compared with 11%" and 6%).

Instant claim 11: The purified complexes were obtained by fractionation of a membrane-free French press lysate (see page 1715, lines 3-4) after growth of the cells at 98° degrees C (see page 1720, materials and methods, col. 2, paragraph 2, line 3), as well as a shift from 102° degrees C to 108° degrees C (see abstract, page 1711), the optimal/normal growth conditions being 59° degrees C (see page 1713, col. 1, paragraph 2).

Purified complexes were obtained by the process of:

Exposing the bacteria to a stress inducing heat shock stimulus (see abstract, temperature shift from 102° degrees C to 108° degrees C (see abstract, page 1711; page 1721, col. 1 "Heat Shock" section), and

Extracting from the heat shocked cells complexes (see Figure 1, and see page 1715, lines 3-4) which are then combined with an aqueous carrier buffer, specifically Tris-NaCl, pH 7.0 (see page 1720, col. 2, paragraph 8 "50 mM Tris-CL pH 7.0, 50 mM NaCl").

Instant claim 12: the purified complexes were combined with an adjuvant (see page 1721, col. 1, paragraph 5 "Freund's complete adjuvant")

Instant claim 13: The purified complexes were combined with an aqueous carrier buffer, specifically Tris-NaCl, pH 7.0 (see page 1720, col. 2, paragraph 8 "50 mM Tris-CL pH 7.0, 50 mM NaCl").

Instant claim 14: the purified complexes were formulated for inducing an immune response in a method that comprised the step of:

administering to an animal purified complexes together with an adjuvant, in an amount effective to induce an immune response (see page 1721, col. 1, paragraph 5 "Antiserum was raised in a male rabbit by injection of a 1:1 (v/v) emulsion of the purified complex in Freund's complete adjuvant").

Phipps et al anticipates the instantly claimed invention as now claimed.

The purification or production of a product by a particular process (i.e. the instant recombinant) does not impart novelty or unobviousness to a product when the product is taught by the prior art. This is particularly true, when the properties of the product are not changed by the process in an unexpected manner. *In re Thorpe*, 227 USPQ 964 (CAFC 1985); *In re Marosi*, 218 USPQ 289, 292-293 (CAFC 1983); and *In re Brown*, 173 USPQ 685 (CCPA 1972). Therefore, even if a particular process used to prepare a product is novel and unobvious over the prior art, the product *per se*, even when limited to the particular process, is unpatentable over the same product taught by the prior art. *In re King*, 107 F.2d 618, 620, 43 USPQ 400, 402 (CCPA 1939); *In re Merz*, 97 F.2d 559, 601, 38 USPQ 143-45 (CCPA 1938); and *United States v. Ciba-Geigy Corp.*, 508 F.supp. 1157, 1171, 211 USPQ 529, 543 (DNJ 1979).

7. The rejection of claims 10-11 rejected under 35 U.S.C. 102(b) as being anticipated by Wawrzynow et al (1995) is traversed on the grounds that the heat shock protein complex of Wawrzynow et al is not disclosed as being able to illicit an immune response, nor is it characterized as being able to stimulate an immune response in a subject.

8. In response to applicant's argument that the complex is not characterized for inducing an immune response, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

1. It is the position of the examiner that ClpX is immunogenic in light of the fact that antibodies were raised to ClpX and ClpX was shown to be immunoreactive with anti-ClpX antibodies in the ELISA immunoassay shown in Figure 6, page 1873, entire ledger narrative. The disclosure of the complex of Wawrzynow et al meets all of the structural requirements of the claims are disclosed in Wawrzynow et al, and would therefore inherently evidence the same or equivalent functional characteristics.

9. The Wawrzynow et al discloses a complex of a heat shock protein that requires ATP for the formation of the complex with a peptide " λO"(see page 1873, Figure 6 (a, b, c); Figure 7-8, page 1874), the complex being in combination with an aqueous carrier (see Figure 6, "PBS buffer" ledger narrative line 1).

The heat shock protein is known as ClpX, and the gene encoding the protein is under heat-shock regulation (see page 1868, col. 1, last two lines) and requires the presence of ATP or

ATP-y-S for efficient interaction with other proteins (see page 1867, col. 1, article summary and page 1868, sentence bridging col. 1 to col. 2 "The clpX gene codes for a truncated member of the Hsp100 family, possessing one ATP binding site as well as a zinc binding motif"). Wawrzynow et al inherently anticipates the instantly claimed invention as now claimed. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. The Court further held that Athis same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.

10. The rejection of claim 10 under 35 U.S.C. 102(a) as being anticipated by Motohashi et al (June 1999), is traversed on the grounds that the reference is directed to eukaryote heat shock protein complexes.

11. It is the position of the examiner that while the reference discusses eukaryote heat shock protein complexes (page 7188, Discussion), the reference goes beyond this to characterize and show heat shock protein complexes in eubacteria, specifically T. thermophilus (see page 7188, col. 1, paragraph 2, second half of paragraph), to include the dnaK region of T. thermophilus that contains 5 genes that encode dnaK-grpA-dnaJ-dafA and clpB (see page 7185, col. 2, Results section) and also discusses E.coli heat shock protein complexes as well.

Double Patenting

12. Maintained: Claims 10, 12 and 17 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3 and 12 of copending

Application No. 10/363,454 is herein maintained as an effective terminal disclaimer was not submitted. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

New Claim Limitations/New Grounds of Rejection

Claim Rejections - 35 USC § 101

13. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

14. Claims 10, 11-13 and 17 have been amended to recite the phrase "one or more endogenous complexes". In light of the fact that the newly amended claims now read on endogenous heat shock protein complexes that naturally occur in nature, specifically in situ (**in situ (in si·tu)** in the natural or normal place; confined to the site of origin without invasion of neighboring tissues), the instantly claimed compositions now encompass bacteria occurring in nature. Bacterial membranes are known adjuvants, and the cytoplasm of bacteria is a naturally occurring aqueous carrier of the endogenous complexes. The claims as amended now read on a product of nature and are directed to and encompasses non-statutory subject matter.

Conclusion

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GINNY PORTNER whose telephone number is (571)272-0862. The examiner can normally be reached on flextime, but usually M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/G. P./
Examiner, Art Unit 1645
February 25, 2008

/Mark Navarro/
Primary Examiner, Art Unit 1645